Serial No. : 10/045.178

Filed: January 11, 2002

Page : 2 of 19

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1-40. (Canceled)

- (Previously presented) A method of treating a subject having a cell proliferative disorder comprising;
 - contacting the subject with a therapeutically effective amount of a retrovirus,
 comprising:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the retroviral genome;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell.

in a pharmaceutically acceptable carrier; and

b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;

wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

42. (Original) The method of claim 41, wherein the subject is a mammal.

Attorney's Docket No.: 06666-022002 / USC 2862B

Applicant : Noriyuki Kasahara et al.

Serial No.: 10/045.178 Filed: January 11, 2002

Page : 3 of 19

43. (Original) The method of claim 42, wherein the mammal is a human.

- (Original) The method of claim 41, wherein the contacting is by in vivo administration of the retrovirus.
- (Original) The method of claim 44, wherein the in vivo administration is by systemic, local, or topical administration.
- 46. (Withdrawn) The method of claim 41, wherein the contacting is by ex vivo administration of the retrovirus.
- 47. (Canceled)
- 48. (Canceled)
- 49. (Previously presented) The method of claim 41, wherein the oncoretroviral polynucleotide sequence is selected from the group consisting of murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Gibbon ape leukemia virus (GALV) and Human Foamy Virus (HFV).
- (Previously presented) The method of claim 49, wherein the MLV is an amphotropic MLV
- 51. (Previously presented) The method of claim 64, wherein the ENV protein is selected from the group consisting of murine leukemia virus (MLV) ENV protein and vesicular stomatitis virus (VSV) ENV protein.

Attorney's Docket No.: 06666-022002 / USC 2862B Applicant : Noriyuki Kasahara et al.

Serial No. : 10/045,178

Filed : January 11, 2002

Page : 4 of 19

52-55. (Canceled)

(Previously presented) The method of claim 41, wherein the cell proliferative disorder is 56.

selected from the group consisting of lung cancer, colon-rectum cancer, breast cancer,

prostate cancer, urinary tract cancer, uterine cancer lymphoma, oral cancer, pancreatic

cancer, leukemia, melanoma, stomach cancer and ovarian cancer.

57. (Canceled)

58. (Previously Presented) The method of claim 41, wherein the LTR of the retrovirus

comprises a tissue-specific promoter sequence.

59. (Currently Amended) The method of claim 58, wherein the fissue-specific promoter

sequence is associated with a probasin promoter sequence or a growth regulatory gene

promoter sequence.

60. (Canceled)

(Previously presented) The method of claim 41, wherein the suicide gene is a thymidine 61.

kinase or a purine nucleoside phosphorylase (PNP).

62. (Canceled)

(Previously presented) The method of claim 41, wherein the retroviral envelope 63.

comprises a chimeric protein.

(Previously presented) The method of claim 63, wherein the chimeric protein comprises 64.

an ENV protein and a targeting polypeptide.

Serial No.: 10/045,178

Filed : January 11, 2002

Page : 5 of 19

 (Previously presented) The method of claim 64, wherein the targeting polypeptide is an antibody, a receptor, or a receptor ligand.

- 66. (Previously presented) A method of treating a subject having a cell proliferative disorder comprising:
 - a) contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long Terminal Repeat (LTR) sequences at the 5' and 3' ends of the oncoretroviral polynucleotide

sequence;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous polynucleotide encodes a suicide gene; and

cis acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and

- b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;
- wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.
- 67. (Previously presented) The method of claim 66, wherein the polynucleotide sequence encoding a retroviral envelope encodes a chimeric protein.

Serial No.: 10/045,178

Filed : January 11, 2002

Page : 6 of 19

68. (Previously presented) The method of claim 67, wherein the chimeric protein comprises

an ENV protein and a targeting polypeptide.

69. (Previously presented) The method of claim 68, wherein the targeting polypeptide is an

antibody, a receptor, or a receptor ligand.

70. (Previously presented) The method of claim 66, wherein the GAG, POL and retroviral

envelope polynucleotide sequences are from murine leukemia virus (MLV) or Moloney

murine leukemia virus (MoMLV).

71. (Previously presented) The method of claim 70, wherein the MoMLV is an amphotropic

MoMLV.

72. (Previously presented) The method of claim 68, wherein the ENV protein is an ecotropic

protein.

73. (Previously presented) The method of claim 68, wherein the ENV protein is selected

from the group consisting of a murine leukemia virus (MoMLV) ENV protein and

vesicular stomatitis virus (VSV) ENV protein.

74. (Canceled)

75. (Previously presented) The method of claim 66, wherein the suicide gene encodes a

thymidine kinase or a purine nucleoside phosphorylase (PNP).

76. (Canceled)

Serial No.: 10/045,178 Filed: January 11, 2002

Page : 7 of 19

77. (Previously presented) The method of claim 66, wherein the regulatory nucleic acid sequence operably linked with the heterologous nucleic acid sequence is selected from the group consisting of a promoter, an enhancer, and an internal ribosome entry site.

- 78. (Previously presented) The method of claim 66, wherein the polynucleotide sequence is contained in a viral particle.
- (Previously presented) The method of claim 66, wherein the polynucleotide sequence is contained in a pharmaceutically acceptable carrier.
- (Previously presented) A method of treating a subject having a cell proliferative disorder comprising:
 - a) contacting the subject with a therapeutically effective amount of a recombinant replication competent murine leukemia virus (MLV), comprising:

an MLV GAG protein;

an MLV POL protein;

an MLV envelope;

an MLV polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the MLV polynucleotide sequence;

- a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell; and
- b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;

wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

Serial No.: 10/045,178

Filed : January 11, 2002

Page : 8 of 19

81. (Previously presented) A method of treating a subject having a cell proliferative disorder comprising:

 a) contacting the subject with a therapeutically effective amount of a recombinant replication competent retrovirus comprising;

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope comprising a chimeric env protein comprising a targeting ligand;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the oncoretroviral polynucleotide sequence;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and

b) contacting the subject with a prodrug which is activated by the expression of the suicide gene;

wherein the cell proliferative disorder is a neoplastic disorder or associated with an overgrowth of connective tissue.

- 82. (Previously presented) A method of treating a subject having a cell proliferative disorder comprising:
 - a) contacting the subject with a therapeutically effective amount of a recombinant retroviral polynucleotide, comprising:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope, wherein said envelope comprises a chimeric env protein comprising a targeting ligand;

Serial No.: 10/045,178 Filed: January 11, 2002

Page : 9 of 19

an oncoretroviral polynucleotide sequence comprising Long Terminal Repeat (LTR) sequences at the 5' and 3' ends of the oncoretroviral polynucleotide; a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous polynucleotide encodes a suicide gene; cis acting polynucleotide sequences involved in reverse transcription, packaging and integration in a target cell; and

b) contacting the subject with a prodrug which is activated by the expression
of the suicide gene;
 wherein the cell proliferative disorder is a neoplastic disorder or associated with an

Claims 83-86 canceled.

- 87. (Previously presented) A method of treating glioblastoma in a subject comprising:
- a) administering a therapeutically effective amount of a retrovirus to the subject, wherein the retrovirus comprises:

a retroviral GAG protein;

overgrowth of connective tissue.

a retroviral POL protein:

a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the retroviral genome;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and

cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and

b) administering a prodrug, which is activated by the expression of the suicide gene, to the subject.

Serial No.: 10/045,178

Filed: January 11, 2002

Page : 10 of 19

88. (Previously presented) The method of claim 87, wherein the regulatory nucleic acid

sequence comprises a tissue-specific promoter sequence.

89. (Previously presented) A method of treating a glioblastoma in a subject comprising:

a) administering a therapeutically effective amount of a recombinant retroviral

polynucleotide to the subject, wherein the recombinant retroviral polynucleotide comprises:

a polynucleotide sequence encoding a GAG protein;

a polynucleotide sequence encoding a POL protein;

a polynucleotide sequence encoding a retroviral envelope;

an oncoretroviral polynucleotide sequence comprising Long Terminal Repeat

(LTR) sequences at the 5' and 3' ends of the oncoretroviral polynocleotide sequence;

a heterologous polynucleotide sequence operably linked to a regulatory nucleic

acid sequence, wherein the heterologous polynucleotide encodes a suicide gene; and

cis acting nucleic acid sequences involved in reverse transcription, packaging and

integration in a target cell; and

administering a prodrug, which is activated by the expression of the suicide gene,

to the subject.

90. (Previously presented) The method of claim 89, wherein the regulatory nucleic acid

sequence comprises a tissue-specific promoter sequence.

91. (Previously presented) A method of treating a glioblastoma in a subject comprising:

a) administering a therapeutically effective amount of a recombinant replication

competent murine leukemia virus (MLV) to the subject, wherein the recombinant replication

competent MLV comprises:

an MLV GAG protein;

an MLV POL protein;

an MLV envelope;

Serial No.: 10/045,178

Filed : January 11, 2002

Page : 11 of 19

ligand;

an MLV polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the MLV polynucleotide sequence;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and

cis-acting nucleic acid sequences necessary for reverse transcription, packaging and integration in a target cell; and

- b) administering a prodrug, which is activated by the expression of the suicide gene, to the subject.
- 92. (Previously presented) The method of claim 91, wherein the regulatory nucleic acid sequence comprises a tissue-specific promoter sequence.
- 93. (Previously presented) A method of treating a glioblastoma in a subject comprising:
- a) administering a therapeutically effective amount of a recombinant replication competent retrovirus to the subject, wherein the recombinant replication competent retrovirus comprises:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope comprising a chimeric env protein comprising a targeting

an oncoretroviral polynucleotide sequence comprising Long-Terminal Repeat (LTR) sequences at the 5' and 3' ends of the oncoretroviral polynucleotide sequence;

a heterologous nucleic acid sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous nucleic acid encodes a suicide gene; and

cis-acting nucleic acid sequences involved in reverse transcription, packaging and integration in a target cell; and

b) administering a prodrug, which is activated by the expression of the suicide gene, to the subject.

Serial No.: 10/045,178

Filed : January 11, 2002

Page : 12 of 19

94. (Previously presented) The method of claim 93, wherein the regulatory nucleic acid sequence comprises a tissue-specific promoter sequence.

- 95. (Previously presented) A method of treating a glioblastoma in a subject comprising:
- a) administering a therapeutically effective amount of a recombinant retroviral polynucleotide to the subject, wherein the recombinant retroviral polynucleotide comprises:
 - a polynucleotide sequence encoding a GAG protein;
 - a polynucleotide sequence encoding a POL protein;
- a polynucleotide sequence encoding a retroviral envelope, wherein said envelope comprises a chimeric env protein comprising a targeting ligand:
- an oncoretroviral polynucleotide sequence comprising Long Terminal Repeat (LTR) sequences at the 5' and 3' ends of the oncoretroviral polynucleotide;
- a heterologous polynucleotide sequence operably linked to a regulatory nucleic acid sequence, wherein the heterologous polynucleotide encodes a suicide gene;
- cis acting polynucleotide sequences involved in reverse transcription, packaging and integration in a target cell; and
- b) administering a prodrug, which is activated by the expression of the suicide gene, to the subject.
- 96. (Previously presented) The method of claim 95, wherein the regulatory nucleic acid sequence comprises a tissue-specific promoter sequence.